

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

Claim 1 (withdrawn). A method of increasing the potency of an anti-microbial agent comprising co-administering to a subject infected with an ABC transporter-mediated multidrug resistant microbe:

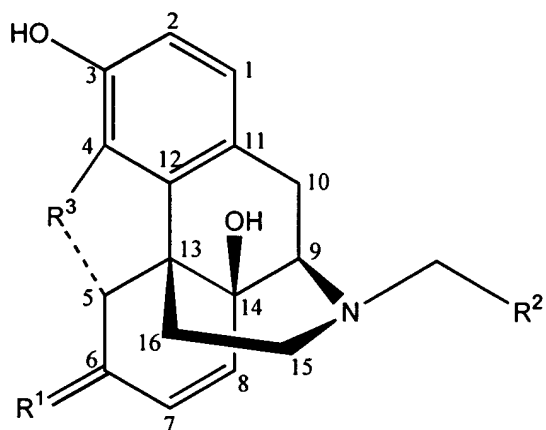
- (a) a dose of an anti-microbial agent, wherein the anti-microbial agent is a substrate of an ABC drug transporter; and
- (b) a dose of an opioid inhibitor of the ABC drug transporter.

Claim 2 (withdrawn). The method of claim 1, wherein the dose of the opioid inhibitor of the ABC drug transporter is sufficient to reduce efflux of the anti-microbial agent from the microbe, increase intracellular concentration of the anti-microbial agent in the microbe, or inhibit a drug transporter of the subject.

Claim 3 (withdrawn). The method of claim 1, wherein the ABC drug transporter is a homologue of human PGP1a.

Claim 4 (withdrawn). The method of claim 1, wherein the anti-microbial agent is one of the group of agents that are penicillins, cephalosporins, cycloserine, vancomycin, bacitracin, the azole antifungal agent, the polyene antifungal agents, the allylaminesthiocarbamates, chloramphenicol, the tetracyclines, erythromycin, clindamycin, the pristamycins, the aminoglycosides, the rifamycins, the quinolones, trimethoprim, the sulfonamides, acyclovir, ganciclovir, zidovudine, lamivudine, daunomycin or doxorubicin.

Claim 5 (withdrawn). The method of claim 1, wherein the opioid inhibitor of the ABC drug transporter is a compound of the formula:



wherein R^1 is CH_2 or O ;

wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and

wherein R^3 is O , CH_2 or NH .

Claim 6 (withdrawn). The method of claim 1, wherein the opioid inhibitor of the ABC drug transporter is nalmefene, naltrexone or naloxone.

Claim 7 (withdrawn). The method of claim 1, wherein the microbe causing the microbial infection is one of the groups of microbes that are *Staphylococcus*, *Streptococcus*, *Micrococcus*, *Peptococcus*, *Peptostreptococcus*, *Enterococcus*, *Bacillus*, *Clostridium*, *Lactobacillus*, *Listeria*, *Erysipelothrix*, *Propionibacterium*, *Eubacterium*, *Corynebacterium*, *Pseudomonas*, *Plasmodium*, *Leishmania*, *Absidia*, *Aspergillus*, *Basidiobolus*, *Blastomyces*, *Candida*, *Coccidioides*, *Conidiobolus*, *Cryptococcus*, *Cunninghamella*, *Histoplasma*, *Mortierella*, *Mucor*, *Paracoccidioides*, *Rhizopus*, *Saksenaea*, , *Acidaminococcus*, *Acinetobacter*, *Aeromonas*, *Alcaligenes*, *Bacteroides*, *Bordetella*, *Branhamella*, *Brucella*, *Calymmatobacterium*, *Campylobacter*, *Cardiobacterium*, *Chromobacterium*, *Citrobacter*, *Edwardsiella*, *Enterobacter*, *Escherichia*, *Flavobacterium*, *Francisella*, *Fusobacterium*, *Haemophilus*, *Klebsiella*, *Legionella*, *Moraxella*, *Morganella*, *Neisseria*, *Pasturella*, *Plesiomonas*, *Proteus*, *Providencia*, *Pseudomonas*, *Salmonella*, *Serratia*, *Shigella*, *Streptobacillus*, *Veillonella*, *Vibrio*, or *Yersinia*.

Claim 8 (withdrawn). The method of claim 1, wherein the opioid inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 9 (withdrawn). A method of increasing the potency of an anti-microbial agent comprising co-administering to a subject infected with an ABC transporter-mediated multidrug resistant microbe:

(a) a dose of an anti-microbial agent, wherein the anti-microbial agent is a substrate of an ABC drug transporter; and

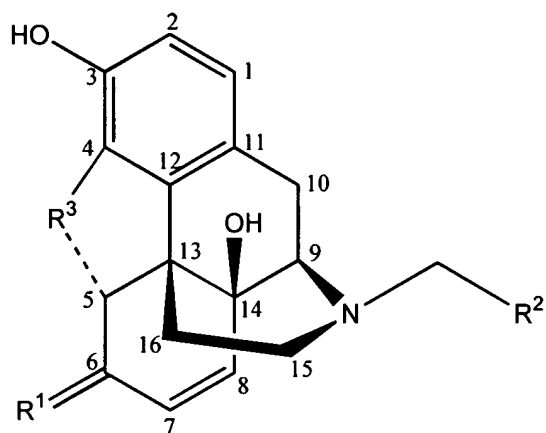
(b) a dose of an opioid inhibitor of the ABC drug transporter.

Claim 10 (withdrawn). The method of claim 9, wherein the dose of the opioid inhibitor of the ABC drug transporter is sufficient to increase the intracellular concentration of the anti-microbial agent in the microbe, reduce efflux of the anti-microbial agent from the microbe, or inhibit a drug transporter of the subject.

Claim 11 (withdrawn). The method of claim 9, wherein the ABC drug transporter is a homologue of human PGP1a.

Claim 12 (withdrawn). The method of claim 9, wherein the anti-microbial agent is one of the groups of agents that are penicillins, cephalosporins, cycloserine, vancomycin, bacitracin, the azole antifungal agent, the polyene antifungal agents, the allylaminesthiocarbamates, chloramphenicol, the tetracyclines, erythromycin, clindamycin, the pristamycins, the aminoglycosides, the rifamycins, the quinolones, trimethoprim, the sulfonamides, acyclovir, ganciclovir, zidovudine, lamivudine, daunomycin or doxorubicin.

Claim 13 (withdrawn). The method of claim 9, wherein the opioid inhibitor of the ABC drug transporter is a compound of the formula:



wherein R¹ is CH₂ or O;

wherein R² is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and

wherein R³ is O, CH₂ or NH.

Claim 14 (withdrawn). The method of claim 9, wherein the opioid inhibitor of the ABC drug transporter is nalmefene, naltrexone or naloxone.

Claim 15 (withdrawn). The method of claim 9, wherein the microbe causing the microbial infection is one of the groups of microbes that are *Staphylococcus*, *Streptococcus*, *Micrococcus*, *Peptococcus*, *Peptostreptococcus*, *Enterococcus*, *Bacillus*, *Clostridium*, *Lactobacillus*, *Listeria*, *Erysipelothrix*, *Propionibacterium*, *Eubacterium*, *Corynebacterium*, *Pseudomonas*, *Plasmodium*, *Leishmania*, *Absidia*, *Aspergillus*, *Basidiobolus*, *Blastomyces*, *Candida*, *Coccidioides*, *Conidiobolus*, *Cryptococcus*, *Cunninghamella*, *Histoplasma*, *Mortierella*, *Mucor*, *Paracoccidioides*, *Rhizopus*, *Saksenaea*, , *Acidaminococcus*, *Acinetobacter*, *Aeromonas*, *Alcaligenes*, *Bacteroides*, *Bordetella*, *Branhamella*, *Brucella*, *Calymmatobacterium*, *Campylobacter*, *Cardiobacterium*, *Chromobacterium*, *Citrobacter*, *Edwardsiella*, *Enterobacter*, *Escherichia*, *Flavobacterium*, *Francisella*, *Fusobacterium*, *Haemophilus*, *Klebsiella*, *Legionella*, *Moraxella*, *Morganella*, *Neisseria*, *Pasteurella*, *Plesiomonas*, *Proteus*, *Providencia*, *Pseudomonas*, *Salmonella*, *Serratia*, *Shigella*, *Streptobacillus*, *Veillonella*, *Vibrio*, or *Yersinia*.

Claim 16 (withdrawn). The method of claim 9, wherein the opioid inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 17 (withdrawn). A composition for treating a microbial infection comprising:

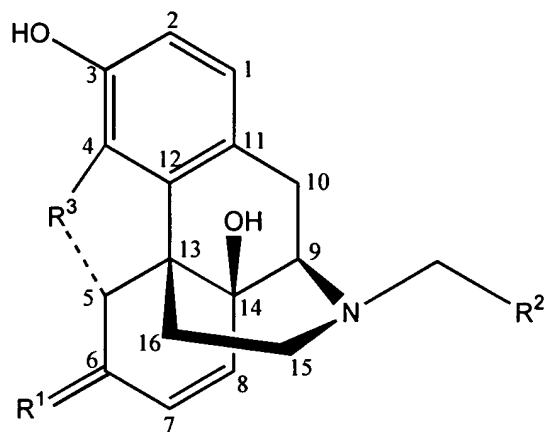
(a) an anti-microbial agent, wherein the anti-microbial agent is a substrate of an ABC drug transporter; and

(b) an opioid inhibitor of the ABC drug transporter.

Claim 18 (withdrawn). The composition of claim 17, wherein the ABC drug transporter is a homologue of human PGP1a.

Claim 19 (withdrawn). The composition of claim 17, wherein the anti-microbial agent is one of the groups of agents that are penicillins, cephalosporins, cycloserine, vancomycin, bacitracin, the azole antifungal agent, the polyene antifungal agents, the allylaminesthiocarbamates, chloramphenicol, the tetracyclines, erythromycin, clindamycin, the pristamycins, the aminoglycosides, the rifamycins, the quinolones, trimethoprim, the sulfonamides, acyclovir, ganciclovir, zidovudine, lamivudine, daunomycin or doxorubicin.

Claim 20 (withdrawn). The composition of claim 17, wherein the opioid inhibitor of the ABC drug transporter is a compound of the formula:



wherein R¹ is CH₂ or O;

wherein R² is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and

wherein R³ is O, CH₂ or NH.

Claim 21 (withdrawn). The composition of claim 17, wherein the opioid inhibitor of the ABC drug transporter is nalmefene, naltrexone or naloxone.

Claim 22 (withdrawn). The composition of claim 17, wherein the microbe causing the microbial infection is one of the groups of microbes that are *Staphylococcus*, *Streptococcus*, *Micrococcus*, *Peptococcus*, *Peptostreptococcus*, *Enterococcus*, *Bacillus*, *Clostridium*, *Lactobacillus*, *Listeria*, *Erysipelothrix*, *Propionibacterium*, *Eubacterium*, *Corynebacterium*, *Pseudomonas*, *Plasmodium*, *Leishmania*, *Absidia*, *Aspergillus*, *Basidiobolus*, *Blastomyces*, *Candida*, *Coccidioides*, *Conidiobolus*, *Cryptococcus*, *Cunninghamella*, *Histoplasma*, *Mortierella*, *Mucor*, *Paracoccidioides*, *Rhizopus*, *Saksenaea*, , *Acidaminococcus*, *Acinetobacter*, *Aeromonas*, *Alcaligenes*, *Bacteroides*, *Bordetella*, *Branhamella*, *Brucella*, *Calymmatobacterium*, *Campylobacter*, *Cardiobacterium*, *Chromobacterium*, *Citrobacter*, *Edwardsiella*, *Enterobacter*, *Escherichia*, *Flavobacterium*, *Francisella*, *Fusobacterium*, *Haermophilus*, *Klebsiella*, *Legionella*, *Moraxella*, *Morganella*, *Neisseria*, *Pasturella*, *Plesiomonas*, *Proteus*, *Providencia*, *Pseudomonas*, *Salmonella*, *Serratia*, *Shigella*, *Streptobacillus*, *Veillonella*, *Vibrio*, or *Yersinia*.

Claim 23 (withdrawn). The composition of claim 17, wherein the opioid inhibitor of the drug transporter is nalmefene.

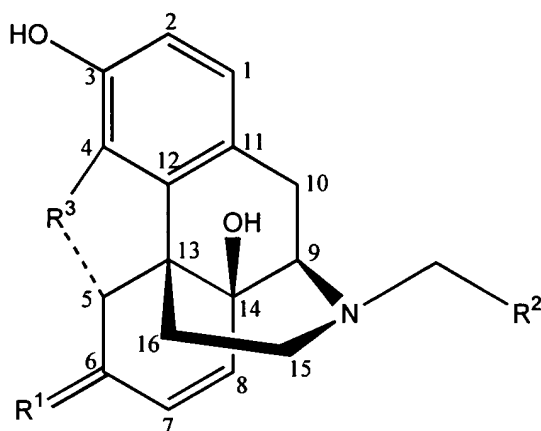
Claim 24 (withdrawn). The composition of claim 17, wherein the opioid inhibitor of the drug transporter is a compound having the pharmacophore defined by:
a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;
a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;
a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and
a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 25 (withdrawn). A method of enhancing the anti-microbial activity of an anti-microbial agent against a microbe comprising:
contacting the microbe with the anti-microbial agent and an opioid inhibitor of an ABC drug transporter in an amount effective to inhibit a drug transporter in the microbe, wherein the microbe expresses an ABC drug transporter and the anti-microbial agent is a substrate of the ABC drug transporter.

Claim 26 (withdrawn). The method of claim 25, wherein the ABC drug transporter is a homologue of human PGP1a.

Claim 27 (withdrawn). The method of claim 25, wherein the anti-microbial agent is one of the groups of agents that are penicillins, cephalosporins, cycloserine, vancomycin, bacitracin, the azole antifungal agent, the polyene antifungal agents, the allylaminesthiocarbamates, chloramphenicol, the tetracyclines, erythromycin, clindamycin, the pristamycins, the aminoglycosides, the rifamycins, the quinolones, trimethoprim, the sulfonamides, acyclovir, ganciclovir, zidovudine, lamivudine, daunomycin or doxorubicin.

Claim 28 (withdrawn). The method of claim 25, wherein the opioid inhibitor of the ABC drug transporter is a compound of the formula:



wherein R^1 is CH_2 or O ;

wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and

wherein R^3 is O , CH_2 or NH .

Claim 29 (withdrawn). The method of claim 25, wherein the opioid inhibitor of the ABC drug transporter is nalmefene, naltrexone or naloxone.

Claim 30 (withdrawn). The method of claim 25, wherein the microbe causing the microbial infection is one of the groups of microbes that are *Staphylococcus*, *Streptococcus*, *Micrococcus*, *Peptococcus*, *Peptostreptococcus*, *Enterococcus*, *Bacillus*, *Clostridium*, *Lactobacillus*, *Listeria*, *Erysipelothrix*, *Propionibacterium*, *Eubacterium*, *Corynebacterium*, *Pseudomonas*, *Plasmodium*, *Leishmania*, *Absidia*, *Aspergillus*, *Basidiobolus*, *Blastomyces*, *Candida*, *Coccidioides*, *Conidiobolus*, *Cryptococcus*, *Cunninghamella*, *Histoplasma*, *Mortierella*, *Mucor*, *Paracoccidioides*, *Rhizopus*, *Saksenaea*, *Acidaminococcus*, *Acinetobacter*, *Aeromonas*, *Alcaligenes*, *Bacteroides*, *Bordetella*, *Branhamella*, *Brucella*, *Calymmatobacterium*, *Campylobacter*, *Cardiobacterium*, *Chromobacterium*, *Citrobacter*, *Edwardsiella*, *Enterobacter*, *Escherichia*, *Flavobacterium*, *Francisella*, *Fusobacterium*, *Haemophilus*, *Klebsiella*, *Legionella*, *Moraxella*, *Morganella*, *Neisseria*, *Pasturella*, *Plesiomonas*, *Proteus*, *Providencia*, *Pseudomonas*, *Salmonella*, *Serratia*, *Shigella*, *Streptobacillus*, *Veillonella*, *Vibrio*, or *Yersinia*.

Claim 31 (withdrawn). The method of claim 25, wherein the opioid inhibitor of the drug transporter is nalmefene.

Claim 32 (withdrawn). The method of claim 25, wherein the opioid inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

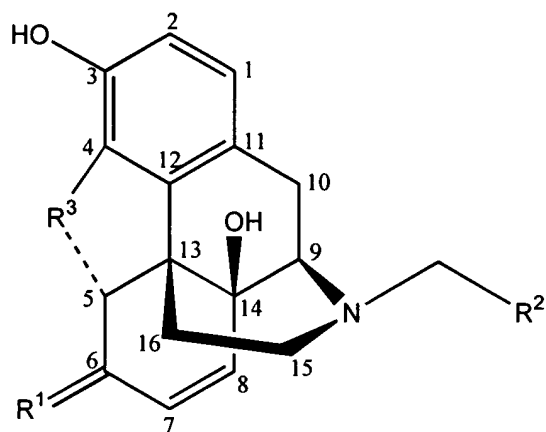
Claim 33 (withdrawn). A method of suppressing growth of a microbe expressing an ABC drug transporter protein comprising:

contacting the microbe with a sub-therapeutic amount of an anti-microbial agent in the presence of an opioid inhibitor of the ABC drug transporter.

Claim 34 (withdrawn). The method of claim 33, wherein the ABC drug transporter is a homologue of human PGP1a.

Claim 35 (withdrawn). The method of claim 33, wherein the anti-microbial agent is one of the groups of agents that are penicillins, cephalosporins, cycloserine, vancomycin, bacitracin, the azole antifungal agent, the polyene antifungal agents, the allylaminesthiocarbamates, chloramphenicol, the tetracyclines, erythromycin, clindamycin, the pristamycins, the aminoglycosides, the rifamycins, the quinolones, trimethoprim, the sulfonamides, acyclovir, ganciclovir, zidovudine, lamivudine, daunomycin or doxorubicin.

Claim 36 (withdrawn). The method of claim 33, wherein the opioid inhibitor of the ABC drug transporter is a compound of the formula:



wherein R^1 is CH_2 or O ;

wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and

wherein R^3 is O , CH_2 or NH .

Claim 37 (withdrawn). The method of claim 33, wherein the opioid inhibitor of the ABC drug transporter is nalmeferene, naltrexone or naloxone.

Claim 38 (withdrawn). The method of claim 33, wherein the microbe is one of the groups of microbes that are *Staphylococcus*, *Streptococcus*, *Micrococcus*, *Peptococcus*, *Peptostreptococcus*, *Enterococcus*, *Bacillus*, *Clostridium*, *Lactobacillus*, *Listeria*, *Erysipelothrix*, *Propionibacterium*, *Eubacterium*, *Corynebacterium*, *Pseudomonas*, *Plasmodium*, *Leishmania*, *Absidia*, *Aspergillus*, *Basidiobolus*, *Blastomyces*, *Candida*, *Coccidioides*, *Conidiobolus*, *Cryptococcus*, *Cunninghamella*, *Histoplasma*, *Mortierella*, *Mucor*, *Paracoccidioides*, *Rhizopus*, *Saksenaea*, , *Acidaminococcus*, *Acinetobacter*, *Aeromonas*, *Alcaligenes*, *Bacteroides*, *Bordetella*, *Branhamella*, *Brucella*, *Calymmatobacterium*, *Campylobacter*, *Cardiobacterium*, *Chromobacterium*, *Citrobacter*, *Edwardsiella*, *Enterobacter*, *Escherichia*, *Flavobacterium*, *Francisella*, *Fusobacterium*, *Haemophilus*, *Klebsiella*, *Legionella*, *Moraxella*, *Morganella*, *Neisseria*, *Pasturella*, *Plesiomonas*, *Proteus*, *Providencia*, *Pseudomonas*, *Salmonella*, *Serratia*, *Shigella*, *Streptobacillus*, *Veillonella*, *Vibrio*, or *Yersinia*.

Claim 39 (withdrawn). The method of claim 33, wherein the opioid inhibitor of the drug transporter is nalmefene.

Claim 40 (withdrawn). The method of claim 33, wherein the opioid inhibitor of the drug transporter is a compound having the pharmacophore defined by:

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;

a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;

a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and

a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

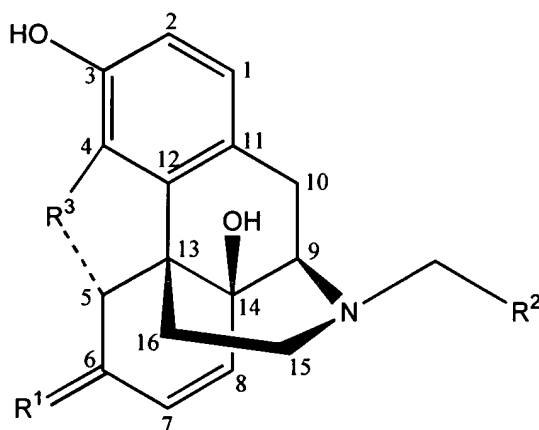
Claim 41 (withdrawn). A method of inhibiting a microbial P-glycoprotein homologue in a patient suffering from a microbial infection comprising administering to the patient a P-glycoprotein inhibiting amount of an inhibitor of an ABC drug transporter, wherein the inhibitor is nalmefene, naltrexone or naloxone, wherein the inhibitor is administered before, with, or after the administration to the patient of a therapeutic or sub-therapeutic amount of an anti-microbial agent.

Claim 42 (withdrawn). The method of claim 41, wherein the ABC drug transporter is a homologue of human PGP1a.

Claim 43 (withdrawn). The method of claim 41, wherein the anti-microbial agent is one of the groups of agents that are penicillins, cephalosporins, cycloserine, vancomycin, bacitracin, the azole antifungal agent, the polyene antifungal agents, the allylaminesthiocarbamates, chloramphenicol, the tetracyclines, erythromycin, clindamycin, the pristamycins, the aminoglycosides, the rifamycins, the quinolones, trimethoprim, the sulfonamides, acyclovir, ganciclovir, zidovudine, lamivudine, daunomycin or doxorubicin.

Claim 44 (withdrawn). The method of claim 41, wherein the microbe causing the microbial infection is one of the groups of microbes that are *Staphylococcus*, *Streptococcus*, *Micrococcus*, *Peptococcus*, *Peptostreptococcus*, *Enterococcus*, *Bacillus*, *Clostridium*, *Lactobacillus*, *Listeria*, *Erysipelothrix*, *Propionibacterium*, *Eubacterium*, *Corynebacterium*, *Pseudomonas*, *Plasmodium*, *Leishmania*, *Absidia*, *Aspergillus*, *Basidiobolus*, *Blastomyces*, *Candida*, *Coccidioides*, *Conidiobolus*, *Cryptococcus*, *Cunninghamella*, *Histoplasma*, *Mortierella*, *Mucor*, *Paracoccidioides*, *Rhizopus*, *Saksenaea*, , *Acidaminococcus*, *Acinetobacter*, *Aeromonas*, *Alcaligenes*, *Bacteroides*, *Bordetella*, *Branhamella*, *Brucella*, *Calymmatobacterium*, *Campylobacter*, *Cardiobacterium*, *Chromobacterium*, *Citrobacter*, *Edwardsiella*, *Enterobacter*, *Escherichia*, *Flavobacterium*, *Francisella*, *Fusobacterium*, *Haemophilus*, *Klebsiella*, *Legionella*, *Moraxella*, *Morganella*, *Neisseria*, *Pasturella*, *Plesiomonas*, *Proteus*, *Providencia*, *Pseudomonas*, *Salmonella*, *Serratia*, *Shigella*, *Streptobacillus*, *Veillonella*, *Vibrio*, or *Yersinia*.

Claim 45 (withdrawn). A method of inhibiting a microbial P-glycoprotein homologue in a patient suffering from a microbial infection comprising administering to the patient a P-glycoprotein inhibiting amount of an inhibitor of an ABC drug transporter, wherein the inhibitor of the ABC drug transporter is a compound of the formula:



wherein R^1 is CH_2 or O;

wherein R^2 is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and

wherein R^3 is O, CH_2 or NH,

wherein the inhibitor of the ABC drug transporter is administered before, with, or after the administration to the patient of an anti-microbial effective amount of an anti-microbial agent.

Claim 46 (withdrawn). The method of claim 45, wherein the anti-microbial agent is one of the groups of agents that are penicillins, cephalosporins, cycloserine, vancomycin, bacitracin, the azole antifungal agent, the polyene antifungal agents, the allylaminesthiocarbamates, chloramphenicol, the tetracyclines, erythromycin, clindamycin, the pristamycins, the aminoglycosides, the rifamycins, the quinolones, trimethoprim, the sulfonamides, acyclovir, ganciclovir, zidovudine, lamivudine, daunomycin or doxorubicin.

Claim 47 (withdrawn). The method of claim 45, wherein the microbe causing the microbial infection is one of the groups of microbes that are *Staphylococcus*, *Streptococcus*, *Micrococcus*, *Peptococcus*, *Peptostreptococcus*, *Enterococcus*, *Bacillus*, *Clostridium*, *Lactobacillus*, *Listeria*, *Erysipelothrix*, *Propionibacterium*, *Eubacterium*, *Corynebacterium*, *Pseudomonas*, *Plasmodium*, *Leishmania*, *Absidia*, *Aspergillus*, *Basidiobolus*, *Blastomyces*, *Candida*, *Coccidioides*, *Conidiobolus*, *Cryptococcus*, *Cunninghamella*, *Histoplasma*, *Mortierella*, *Mucor*, *Paracoccidioides*, *Rhizopus*, *Saksenaea*, , *Acidaminococcus*, *Acinetobacter*, *Aeromonas*, *Alcaligenes*, *Bacteroides*, *Bordetella*, *Branhamella*, *Brucella*, *Calymmatobacterium*, *Campylobacter*, *Cardiobacterium*, *Chromobacterium*, *Citrobacter*, *Edwardsiella*, *Enterobacter*, *Escherichia*, *Flavobacterium*, *Francisella*, *Fusobacterium*, *Haemophilus*, *Klebsiella*, *Legionella*, *Moraxella*, *Morganella*, *Neisseria*, *Pasteurella*, *Plesiomonas*, *Proteus*, *Providencia*, *Pseudomonas*, *Salmonella*, *Serratia*, *Shigella*, *Streptobacillus*, *Veillonella*, *Vibrio*, or *Yersinia*.

Claim 48 (currently amended). A composition comprising:

- (a) an opioid inhibitor of an ATP-binding cassette (ABC) drug transporter; and
- (b) **a sub-therapeutic amount of** an anti-microbial agent,

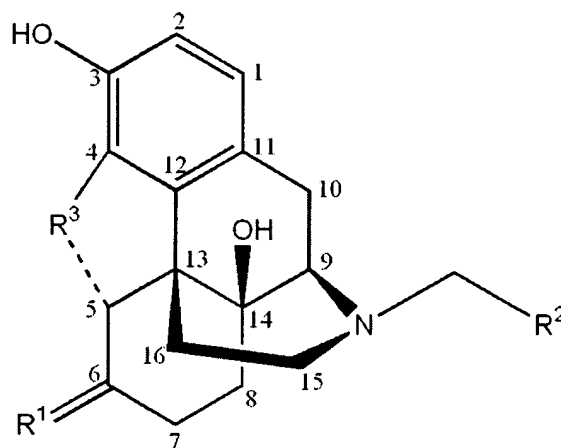
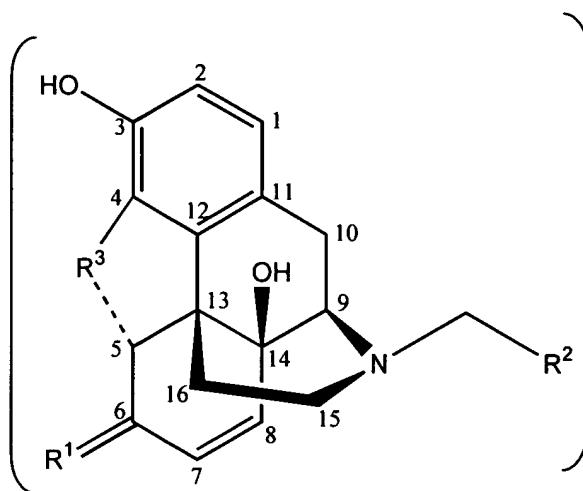
wherein the opioid inhibitor of the ABC drug transporter is capable of inhibiting a drug transporter protein[.]

~~wherein the microbe causing the microbial infection is one of the groups of microbes that are Staphylococcus, Streptococcus, Micrococcus, Peptococcus, Peptostreptococcus, Enterococcus, Bacillus, Clostridium, Lactobacillus, Listeria, Erysipelothrix, Propionibacterium, Eubacterium, Corynebacterium, Pseudomonas, Plasmodium, Leishmania, Absidia, Aspergillus, Basidiobolus, Blastomyces, Candida, Coccidioides, Conidiobolus, Cryptococcus, Cunninghamella, Histoplasma, Mortierella, Mucor, Paracoccidioides, Rhizopus, Saksenaea, Acidarninococcus, Acinetobacter, Aeromonas, Alcaligenes, Bacteroides, Bordetella, Branhamella, Brucella, Calymmatobacterium, Carnpylobacter, Cardiobacterium, Chromobacterium, Citrobacter, Edwardsiella, Enterobacter, Escherichia, Flavobacterium, Francisella, Fusobacterium, Haermophilus, Klebsiella, Legionella, Moraxella, Morganella, Neisseria, Pasturella, Plesiornonas, Proteus, Providencia, Pseudomonas, Salmonella, Serratia, Shigella, Streptobacillus, Veillonella, Vibrio, or Yersinia.~~

Claim 49 (original). The composition of claim 48, wherein the ABC drug transporter is a homologue of human PGP1a.

Claim 50 (original). The composition of claim 48, wherein the anti-microbial agent is one of the groups of microbes that are penicillins, cephalosporins, cycloserine, vancomycin, bacitracin, the azole antifungal agent, the polyene antifungal agents, the allylaminesthiocarbamates, chloramphenicol, the tetracyclines, erythromycin, clindamycin, the pristamycins, the aminoglysides, the rifamycins, the quinolones, trimethaprim, the sulfonamides, acyclovir, ganciclovir, zidovudine, lamivudine, daunomycin and doxorubicin.

Claim 51 (currently amended). The composition of claim 48, wherein the opioid inhibitor of the ABC drug transporter is a compound of the formula:



wherein R¹ is CH₂ or O;

wherein R² is a cycloalkyl, unsubstituted aromatic, alkyl or alkenyl; and

wherein R³ is O, CH₂ or NH.

Claim 52 (original). The composition of claim 48, wherein the opioid inhibitor of the ABC drug transporter is nalmefene, naltrexone or naloxone.

Claim 53. Cancelled.

Claim 54 (original). The composition of claim 48, wherein the opioid inhibitor of the drug transporter is nalmefene.

Claim 55 (original). The composition of claim 48, wherein the opioid inhibitor of the drug transporter is a compound having the pharmacophore defined by:

- a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 3 of naltrexone;
- a hydrogen bonding moiety at a three-dimensional location corresponding to the hydroxyl at position 14 of naltrexone;
- a hydrophobic moiety at a three-dimensional location corresponding to the cyclopropyl moiety appended to the nitrogen of naltrexone; and
- a region of electron density at a three-dimensional location corresponding to the ethylene moiety at 6-position of naltrexone.

Claim 56 (withdrawn). A method of identifying a compound for improved treatment of microbial infections comprising:

- (a) identifying an anti-microbial agent;
 - (b) assaying the ability of the therapeutic agent to be transported across a membrane by an ABC protein; and
 - (c) repeating the transport assay to determine whether addition of an opioid inhibitor of an ABC drug transporter inhibits transport of the therapeutic agent across the membrane,
- whereby the compound that is transported by an ABC protein and whose ABC protein-mediated transport is inhibited by the opioid inhibitor of the ABC drug transporter is identified.

Claim 57 (withdrawn). A method of enhancing the potency of an anti-microbial agent identified by the method of claim 56 comprising:

- co-administering a therapeutic amount of the anti-microbial agent and an amount of an opioid inhibitor of an ABC drug transporter capable of inhibiting a drug transporter, wherein the amount of the opioid inhibitor of the ABC drug transporter is sufficient to reduce transport of the anti-microbial agent across a biological membrane.

Claim 58 (withdrawn). A method for screening for an opioid inhibitor of an ABC drug transporter, comprising determining whether a potential opioid inhibitor

inhibits growth of a microbial cell in the presence of sub-therapeutic amount of anti-microbial agent,

wherein the microbial cell expresses an ABC drug transporter, and

wherein said determining comprises comparing the growth of the microbial cell which expresses the ABC drug transporter, with growth of a second microbial cell which does not produce the ABC drug transporter, wherein the first and second microbial cells are grown in the presence of the sub-therapeutic amount of the anti-microbial agent.

Claim 59 (withdrawn). A method for screening for an opioid inhibitor of an ABC drug transporter, comprising:

contacting a potential opioid inhibitor of an ABC drug transporter protein with the ABC drug transporter protein in the presence of a compound that is nalmefene, naltrexone or naloxone, wherein the compound is detectably labeled;

measuring the amount of detectably labeled compound bound to the ABC drug transporter; and

comparing the measured amount to the amount of detectably labeled compound bound by the ABC drug transporter when the drug transporter is contacted with the compound alone,

whereby a measured amount lower than the amount of compound bound to the ABC drug transporter when contacted alone identifies an opioid inhibitor of the ABC drug transporter.

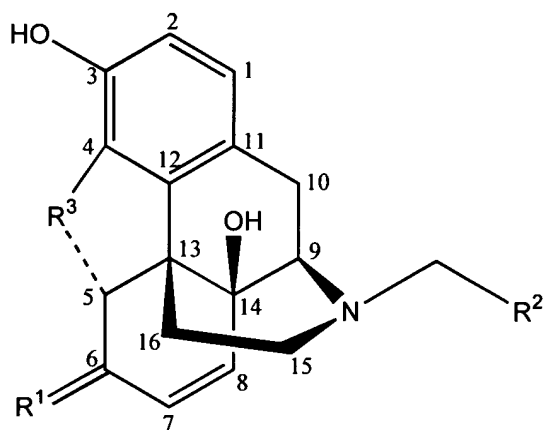
Claim 60 (withdrawn). The method of claim 59, wherein the potential opioid inhibitor of the ABC drug transporter is nalmefene.

Claim 61 (withdrawn). A method of treating a microbial infection in a subject, comprising administering to the subject suffering from the infection an anti-microbial agent and an ABC drug transporter inhibitor in an amount sufficient to increase the intracellular concentration of the anti-microbial agent in the microbe,

wherein the ABC drug transporter inhibitor increases the susceptibility of the microbe to the anti-microbial agent, and

wherein the ABC drug transporter inhibitor is nalmefene, naltrexone or naloxone.

wherein the ABC drug transporter inhibitor is a compound of the formula:



wherein R³ is O, CH₂ or NH.

Claim 63 (new): The composition of claim 48, wherein the anti-microbial agent is adapted to inhibit a microbe selected from *Staphylococcus*, *Streptococcus*, *Micrococcus*, *Peptococcus*, *Peptostreptococcus*, *Enterococcus*, *Bacillus*, *Clostridium*, *Lactobacillus*, *Listeria*, *Erysipelothrix*, *Propionibacterium*, *Eubacterium*, *Corynebacterium*, *Pseudomonas*, *Plasmodium*, *Leishmania*, *Absidia*, *Aspergillus*, *Basidiobolus*, *Blastomyces*, *Candida*, *Coccidioides*, *Conidiobolus*, *Cryptococcus*, *Cunninghamella*, *Histoplasma*, *Mortierella*, *Mucor*, *Paracoccidioides*, *Rhizopus*, *Saksenaea*, , *Acidaminococcus*, *Acinetobacter*, *Aeromonas*, *Alcaligenes*, *Bacteroides*, *Bordetella*, *Branhamella*, *Brucella*, *Calymmatobacterium*, *Campylobacter*, *Cardiobacterium*, *Chromobacterium*, *Citrobacter*, *Edwardsiella*, *Enterobacter*,

Escherichia, Flavobacterium, Francisella, Fusobacterium, Haemophilus , Klebsiella, Legionella, Moraxella, Morganella, Neisseria, Pasturella, Plesiomonas, Proteus, Providencia, Pseudomonas, Salmonella, Serratia, Shigella, Streptobacillus, Veillonella, Vibrio, or Yersinia.